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## **Respiratory load perception in overweight and asthmatic children**

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### **Author contributions**

All experimental work was undertaken within the Department of Respiratory Medicine, King's College London Denmark Hill campus. VM and GFR conceived and designed the project. LW acquired the data. All authors contributed to data analysis and interpretation, drafted the work, approved the final version of the manuscript and agree to be accountable for all aspects of the work. All authors qualify for authorship; all those who qualify for authorship are listed.

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## **Abstract**

Overweight asthmatic children report greater symptoms than normal weight asthmatics, despite comparable airflow obstruction. This has been widely assumed to be due to heightened perception of respiratory effort.

Three groups of children (healthy weight controls, healthy weight asthmatics, overweight asthmatics) rated perceived respiratory effort throughout an inspiratory resistive loading protocol. Parasternal intercostal electromyogram was used as an objective marker of respiratory load; this was expressed relative to tidal volume and reported as a ratio of the baseline value (neuroventilatory activity ratio (NVEAR)). Significant increases in perception scores ( $p < 0.0001$ ), and decreases in NVEAR ( $p < 0.0001$ ) were observed from lowest to highest resistive load. Higher BMI increased overall perception scores, with no influence of asthma or BMI-for-age percentile on the resistance-perception relationships.

These data, indicating elevated overall respiratory effort in overweight asthmatic children but comparable responses to dynamic changes in load, suggest that the greater disease burden in overweight asthmatic children may be due to altered respiratory mechanics associated with increased body mass.

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Key words: Obesity, asthma, child, breathlessness perception

## **1. Introduction**

Asthma is one of the most common chronic conditions of childhood, with a lifetime prevalence of 27.7% in 6-7 year olds and 19.9% in 13-14 year olds in English-speaking countries worldwide (Lai et al., 2009). A strong incident link between excess weight and asthma is well recognised, though the mechanisms underlying this connection remain poorly understood (Rasmussen and Hancox, 2014, Dixon and Poynter, 2016). The prevalence of both overweight and asthma have increased markedly in recent decades (Wang and Lobstein, 2006), and while rates of asthma may have reached a plateau in Western societies (Toelle and Marks, 2005), overweight and obesity is expected to continue to rise. Clinical management of concomitant asthma and overweight is therefore likely to continue to present a significant burden to clinicians.

Despite no differences in objective measures of lung disease severity, coexistent asthma and obesity is associated with higher asthma symptom scores (Sah et al., 2013), greater use of short-acting bronchodilators (Belamarich et al., 2000), increased healthcare utilisation (Carroll et al., 2007) and poorer health-related quality of life (van Gent et al., 2007). Obese children with asthma report higher levels of non-specific breathlessness (Sah et al., 2013) and tend to overestimate the magnitude of airflow obstruction (Kopel et al., 2010). It could be hypothesised, therefore, that overweight or obese children with asthma have heightened perception of respiratory symptoms, although the although the elastic (resulting from reduced chest wall compliance) and threshold (from elevated intra-abdominal pressure, distal gas trapping and intrinsic positive end expiratory pressure) loads

imposed on the respiratory system by obesity itself may contribute to the greater disease burden in obese and overweight children with asthma.

Differences in respiratory load perception have been studied previously in children by investigating subjects' rating of breathlessness or respiratory effort during the application of extrinsic or intrinsic loads (Davenport and Kifle, 2001, Julius et al., 2002). Using an objective marker of response to respiratory load against which to compare subjective scores allows further evaluation of the perception of changing respiratory effort. Measurement of respiratory muscle activity via the parasternal intercostal electromyogram (EMGpara) has been shown to be a valid marker of changing respiratory load in adults (Reilly et al., 2013, Steier et al., 2009) and both healthy and wheezy children (MacBean et al., 2016a). Measurement of EMGpara alongside subjective reports of perceived load allows any hyper-perception to be differentiated from physiological responses to respiratory load.

The purpose of the current study was, therefore, to investigate any differences in respiratory load perception between overweight children with asthma and healthy weight asthmatic and non-asthmatic counterparts, with additional validation of any differences, or lack thereof, quantified by objective measurement of respiratory load *via* EMGpara.

These data have been previously presented in the form of an abstract (MacBean et al., 2016b).

## **2. Methods**

### *2.1 Ethical approval*

The study was granted ethical approval by the National Research Ethics Committee London – Dulwich and conformed to the principles of the Declaration of Helsinki. Parents/guardians of all participants gave informed written consent and assent was obtained from children.

### *2.2 Participant identification and classification*

Children were recruited from databases of previous research participants and from respiratory clinics operating at King's College Hospital. Children were classed as asthmatic if they had a physician diagnosis of asthma and were being prescribed preventative medication (inhaled corticosteroids and/or leukotriene receptor antagonists). Classification of normal weight or overweight was based on World Health Organisation (WHO) BMI-for-age percentiles using WHO Anthro Plus software using the data of de Onis *et al* (de Onis et al., 2007), with overweight classified as a BMI-for-age above the 85<sup>th</sup> percentile and normal weight as BMI-for-age between 2<sup>nd</sup>-85<sup>th</sup> percentile. All children had to be free of any additional cardiac, respiratory or neurological disorder, or recent respiratory illness (within the preceding six weeks). No *a priori* sample size calculation was undertaken due to the exploratory nature of the study.

### *2.3 Pulmonary function tests*

Spirometry and body plethysmography was undertaken in accordance with international criteria. Values for forced expiratory volume in one second (FEV<sub>1</sub>),

forced vital capacity (FVC), total lung capacity (TLC), inspiratory capacity (IC), functional residual capacity (FRC), residual volume (RV) and RV/TLC ratio were compared against reference values (Quanjer et al., 2012, Rosenthal et al., 1993, Zapletal et al., 1977) and expressed as standardised residuals (z-scores).

#### *2.4 Inspiratory resistive loading*

Inspiratory resistive loads were applied using a MicroMedical Respiratory Muscle Analyser (MicroRMA, MicroMedical, UK). The device was pre-programmed to provide seven levels of inspiratory resistance: 1.0, 1.5, 2.3, 3.0, 4.0, 5.5 and 7.0 kiloPascals per litre per second (kPa/l/s). Each resistance was applied for ten breaths and repeated at least three times. Resistances were applied in a pre-determined order that differed between sets to prevent pattern recognition.

#### *2.5 Load perception*

Perception of inspiratory effort was assessed using a 100mm visual analogue scale (VAS) with anchor points at 0cm ("no difficulty at all") and 100mm ("impossible"), and the Pictorial Children's Effort Rating Table (PCERT), (Yelling et al., 2002). Children were asked the question "how difficult was it to breathe?", and asked to rate their perception of respiratory effort first by drawing a line on the VAS then pointing to a step on the PCERT.

#### *2.6 Respiratory flow, tidal volume and airway pressure*

Respiratory flow was recorded using a pneumotachograph (Hans Rudolph Inc, Kansas City, USA) attached proximally to a flanged mouthpiece and distally to the

MicroRMA device. The pressure drop across the pneumotachograph was measured using a differential pressure transducer (Spirometer, ADInstruments, Sydney, Australia). Mouth pressure was recorded from a side arm incorporated into the pneumotachograph and detected using a differential pressure transducer (MP45, Validyne, Northridge, CA, USA) and associated carrier-demodulator amplifier (CD280, Validyne, Northridge, CA, USA). Pressure and flow were recorded throughout the inspiratory loading using LabChart software (version 7.2, ADInstruments, Colorado Springs, USA) with an analogue to digital sampling frequency of 100Hz (PowerLab 8SP, ADInstruments, Sydney, Australia). Tidal volume was derived via digital integration of the flow signal and expressed as ml per kg of predicted body weight (ml/kg<sub>PBW</sub>) to allow comparison between subjects.

## *2.7 Parasternal intercostal electromyography*

EMGpara was recorded using surface electrodes (Kendall Arbo, Tyco Healthcare, Neustadt Donau, Germany) placed over the second intercostal space directly adjacent to the sternal edge bilaterally, with a reference electrode on the acromion process of the scapula. Signals were amplified (gain 1,000) and band pass filtered between 10 and 2,000 Hertz (Hz, 1902 biomedical amplifier, Cambridge Electronic Design, Cambridge, UK). EMGpara signals were acquired alongside respiratory flow and pressure with an analogue-to-digital sampling rate of 4kHz. An additional adaptive mains filter was applied via the analogue to digital converter, and post-acquisition digital band-pass filtering of 10 to 1,000Hz applied by the LabChart acquisition software. EMGpara signals were converted to root mean square (RMS) using a moving window of 50ms for analysis. EMGpara activity occurring between



QRS complexes was selected and the mean peak RMS EMGpara per breath calculated for each resistance. The first breath of each resistance was excluded from EMGpara analysis to eliminate the influence of abnormal responses to load imposition. To eliminate the confounding influence of changing tidal volumes on EMGpara values, EMGpara was expressed relative to the tidal volume for each breath, described as neuroventilatory efficiency (NVE) with units ml/kg<sub>PBW</sub>/μV. NVE at each resistive load was expressed as a ratio of that at baseline (NVE activity ratio (NVEAR)), similar to the method described by Maarsingh *et al* (2002).

## 2.8 Protocol

Baseline recordings of EMGpara, respiratory flow, tidal volume and mouth pressure were recorded for a period of five minutes with the subject seated comfortably in a supportive chair with arms relaxed. The resistive loading device was then attached to the distal side of the pneumotachograph system. Four breaths with no added load were given initially to allow the subject time to acclimatise to the device, followed by ten breaths at the pre-determined resistance. Subjects received verbal indication prior to the first loaded breath to ensure they were aware of the resistance to be rated. After each set of ten loaded breaths, the mouthpiece was removed and the child asked to rate their load perception. This was repeated for all seven programmed resistances, with the full set of seven repeated at least three times. The first set of seven resistances was treated as a practice with the data not included in the analysis.

Pulmonary function tests were performed following completion of the resistive loading protocol. This order was selected in order to avoid the potential for biasing of children's perception or alteration of neural respiratory drive by the manoeuvres required for spirometry and body plethysmography.

## 2.9 *Statistical analysis*

Data were analysed using SPSS (Version 22.0, IBM Corp, Armonk, NY, USA). Non-parametric statistics were used throughout due to the sample size. Comparisons between groups were performed using Kruskal-Wallis tests for continuous data and Fisher's exact test for categorical variables. Mann-Whitney tests were performed to evaluate significance of changes in perception scores and NVE data. Linear mixed model analysis (LMM) was subsequently performed to examine the changes in both perception scores and NVE with increasing resistance, and thereafter to determine the influence of asthma status (treated as a binary variable) and degree of overweight (treated as a continuous variable using BMI-for-age percentile). LMM is an extension of multiple regression, allowing irregularly spaced serial data for individuals to be combined into a single linear regression model, providing estimates of both longitudinal individual changes and group patterns (West, 2009). NVEAR was log-transformed to ensure homoscedasticity of model residuals.

A number of models were constructed:

VAS as the dependent variable; fixed effects: resistance, presence of asthma, BMI-for-age percentile, intercept term; random effect: resistance.

NVEAR as the dependent variable; fixed effects: resistance, presence of asthma, BMI-for-age percentile; random effect: resistance. An intercept term was not included in this model as NVEAR data was expressed relative to the baseline value and thus anchored at a value of one.

Both models using VAS as the dependent variable were also performed with PCERT as the dependent variable.

### **3. Results**

A total of 27 children were studied, nine in each of the three groups (healthy weight controls, healthy weight asthmatics, overweight asthmatics). Subject characteristics are shown in Table 1, with additional data regarding raw values for pulmonary function included within the online supplementary material. Greater airflow obstruction was observed in the overweight asthma group, although the group overall remained within normal limits. EMGpara data could not be consistently obtained in three of the nine overweight children due to attenuation of the EMGpara signal by chest wall adipose tissue.

	<b>Controls (n=9)</b>	<b>Normal weight asthma (n=9)</b>	<b>Overweight asthma (n=9)</b>	<b>p value</b>
<b>Age</b>	10.92 (10.77 – 12.13)	10.77 (9.00 – 13.58)	12.13 (10.98 – 13.17)	0.667
<b>Sex (male : female)</b>	3 : 6	3 : 6	3 : 6	1.00
<b>Height (cm)</b>	152.7 (142.7 – 163.1)	147.7 (129.1 – 164.0)	156.7 (155.8 – 161.1)	0.327
<b>Weight (kg)</b>	32.8 (31.5 – 45.1)	35.7 (30.1 – 52.1)	55.4 (52.2 – 68.1)	0.008*†
<b>BMI-for-age percentile (%)</b>	39.0 (21.0 – 51.5)	61.1 (32.0 – 73.8)	97.0 (94.0 – 97.9)	<0.001*†
<b>FEV<sub>1</sub> (z score)</b>	0.51 (0.10 – 0.75)	0.88 (0.39 – 1.27)	-0.98 (-1.2 – -0.44)	0.016*†
<b>FVC (z score)</b>	0.57 (0.14 – 0.67)	1.27 (0.56 – 1.62)	0.01 (-0.87 – 1.09)	0.076
<b>FEV<sub>1</sub>/FVC ratio (z score)</b>	0.53 (0.19 – 0.61)	-0.31 (-1.08 – 0.17)	-1.18 (-1.27 – -1.02)	0.015*†
<b>TLC (z score)</b>	0.04 (-0.65 – 0.48)	0.56 (0.25 – 1.83)	-1.29 (-1.66 – -0.54)	0.055
<b>IC (z score)</b>	-0.28 (-2.05 – -0.01)	-0.17 (-1.43 – 0.38)	-0.19 (-0.49 – 0.27)	0.518
<b>FRC (z score)</b>	0.18 (-0.33 – 0.38)	0.00 (-0.58 – 0.49)	-1.72 (-2.44 – -0.82)	0.017*†
<b>RV (z score)</b>	-0.43 (-1.02 – -0.29)	-0.10 (-0.25 – 0.00)	-0.79 (-1.24 – 0.51)	0.643
<b>RV/TLC ratio (z score)</b>	-0.09 (-0.85 – 0.30)	-0.17 (-0.67 – 0.17)	0.13 (-0.82 – 0.44)	0.883

Table 1 Subject characteristics. All data are shown as median (IQR). \*significant difference between control and overweight asthmatic subjects, † significant difference between healthy weight asthmatics and overweight asthmatics.

Significant increases in both VAS (Table 2 and Figure 1) and PCERT (Table 2 and Figure 2) were observed from lowest to highest resistance. Significant concomitant decreases in NVEAR were also observed (Table 2 and Figure 3).

	<b>Lowest resistance level</b>	<b>Highest resistance level</b>	<b>p value</b>
<b>VAS (mm)</b>	8.55 (4.0 – 19.0)	73.21 (44.63 – 80.88)	<0.0001
<b>PCERT (AU)</b>	1.59 (1.42 – 2.75)	7.25 (5.25 – 8.5)	<0.0001
<b>NVEAR (AU)</b>	0.89 (0.71 – 1.09)	0.50 (0.44 – 0.59)	<0.0001

Table 2 Changes in perception scores and neural respiratory drive from lowest to highest resistance in 27 children undergoing inspiratory resistive loading. VAS: visual analogue scale; PCERT: Pictorial Children's Effort Rating Table; NVEAR: neuroventilatory efficiency activity ratio.

Linear mixed model analysis was performed to examine the changes in both perception scores and NVE with increasing resistance, and thereafter to determine the influence of asthma status and degree of overweight. Baseline VAS was not significantly different from zero in the normal weight groups (1.76 (95% CI -5.72 – 9.23)mm,  $p=0.643$ ). PCERT was significantly greater than zero (1.29 (0.68 – 1.91)AU,  $p<0.001$ ), but this was by virtue of the fact that the lowest possible score on the

PCERT scale is one. Increasing resistance was associated with an increase in VAS (7.90mm per 1kPa/L/s, 95% CI 3.85 – 11.95,  $p<0.001$ ) and in PCERT (0.69AU/kPa/L/s, 95% CI 0.38 – 1.00,  $p<0.001$ ).

The presence of asthma had no influence on the relationship between VAS or PCERT and increasing resistance ( $p=0.488$  and  $p=0.884$  respectively). Increasing BMI-for-age percentile was associated with a higher intercept value for both VAS (0.19 (0.07 – 0.31)mm,  $p=0.003$ ) and PCERT (0.01 (0.003 – 0.02),  $p=0.01$ ), indicating a relationship between degree of overweight and overall perception scores (increasing by 0.19mm (VAS) or 0.01 AU (PCERT) per percentage point increase in BMI-for-age). There was no effect of BMI-for-age on the slope of VAS or PCERT *versus* resistance ( $p=0.747$  and  $p=0.978$  respectively).

Increasing resistance was significantly associated with reductions in neuroventilatory efficiency (slope -0.06 (-0.11 – -0.01)AU/kPa/L/s,  $p=0.032$ ). There was, however, no effect of BMI-for-age or the presence of asthma on the slope of the resistance *versus* logNVEAR relationship ( $p$  values all  $>0.44$ ) indicating no between-group differences in objective response to increasing inspiratory load.

#### **4. Discussion**

This study is the first to investigate the influence of asthma and overweight on respiratory load perception in children. We have demonstrated no differences in load perception or physiological responses to increasing respiratory load between healthy weight non-asthmatic, healthy weight asthmatic or overweight asthmatic children. We did however note an effect of BMI on the overall value for perception scores, suggesting that adiposity may be associated with chronic elevation of perceived respiratory effort.

Although our study comprised a relatively small sample size with nine subjects in each of the three groups, we adopted a rigorous methodology within the constraints imposed by the young study population. We used a servo-controlled external inspiratory loading device, which maintained the imposed load regardless of any changes in inspiratory flow. Through the use of a familiarisation round at the start of the protocol (the data from which were discarded), randomisation of the order of the imposed loads and repetition of the protocol, the risk of anomalous results was reduced. Following pilot studies (data not shown) the PCERT was adopted in addition to the VAS to ensure all subjects were able to accurately rate perceived inspiratory load. As a consequence no data from the main study were discarded due to exaggerated perception scores.

In addition, the use of linear mixed effects modelling to analyse the data allowed all relevant variables, including repeated observations, to be included in a single robust model. The technique is also tolerant of missing data, meaning that the subjects for



whom EMGpara data could not be obtained could still be retained in the overall model. Such an approach strengthens the results of the study by avoiding inference drawn from multiple univariate analyses and thereby minimising the risk of type I errors.

One weakness of our study is the lack of an overweight, non-asthmatic comparator group. While the inclusion of such a group would have been beneficial, we did not have access to overweight or obese children without comorbidities. Although the statistical analysis techniques we adopted allowed the modelling of the independent contributions of body mass index and asthma status, future studies should seek to include all four groups (healthy weight and overweight asthmatic and non-asthmatic children).

Respiratory load perception has been extensively studied in asthmatic children. Children with a history of life-threatening asthma have been shown to demonstrate blunted load perception, which is thought to contribute to delayed recognition of clinical deterioration and predispose to critical asthma episodes (Davenport and Kifle, 2001, Julius et al., 2002, Kifle et al., 1997). Those without a history of life-threatening asthma are generally thought to exhibit load perception comparable to that of healthy subjects, though with wide inter-individual variation (Kifle et al., 1997, Baker et al., 2000, Banzett et al., 2000, Turcotte et al., 1990). The results of our study are in agreement with these previous findings, in that no differences in load perception were observed between the normal weight asthmatic and the healthy subjects.

Analysis demonstrated a significant elevation in the overall perception scores for the overweight asthmatic group compared to the normal weight healthy and asthmatic groups, as indicated by a higher overall value and no difference in slope. This was related to the degree of BMI elevation, with a mean increase in VAS score of 0.19mm per percentage point increase in BMI-for-age, and 0.01 unit increase in PCERT per BMI-for-age percentile. The consistently higher values of perception scores for the overweight group may provide some insight into the reported higher symptom scores and poorer treatment responses in overweight patients with asthma. The pulmonary function testing results of our overweight group showed changes consistent with the known impact of elevated body mass, including reduced values for FRC and TLC. Breathing at lower lung volumes increases the load on the respiratory system by placing the lung at a less advantageous position on the pressure-volume curve. Together with the elevated intra-abdominal pressure known to occur in obesity placing a threshold load on the diaphragm during inspiration (Steier et al., 2014), overall respiratory system load is elevated in obesity. Elevated neural respiratory drive at rest in obese subjects has previously been demonstrated (Steier et al., 2009). Although we measured neural respiratory drive in the current study using EMGpara, we were unable to compare baseline EMGpara values due to the filtering effect of chest wall adipose tissue. While this can be overcome by normalising the resting signal to that obtained during a maximal inspiratory effort, we have shown that this cannot be reliably performed by pediatric subjects (MacBean et al., 2016a). In order to examine stepwise change we therefore expressed neural respiratory drive relative to baseline, as per the approach of

Maarsingh *et al* (2002), while also accounting for changes in breathing pattern through the use of neuroventilatory efficiency. No differences were observed between groups with respect to the objective responses to increasing inspiratory resistance, though we measured only one index of neural respiratory drive. While EMG<sub>para</sub> is known to be strongly related to diaphragm activity, the patterns of activation of the diaphragm and parasternal intercostals are not identical, particularly under conditions of higher load (Reilly *et al.*, 2011). It is possible that differential recruitment of the parasternal intercostal muscles and diaphragm, along with differences in activation of accessory muscles of inspiration, may occur and indeed may vary between groups. These would not be represented by EMG<sub>para</sub> alone, and future studies may elect to include more comprehensive measures of NRD. Such studies may be better undertaken in adult populations, particularly if incorporating measurement of crural diaphragm EMG *via* oesophageal catheter.

Few previous studies examining symptom reports in overweight asthmatic subjects have undertaken detailed physiological assessment of pulmonary function. The use of measures of airflow obstruction alone (through the use of FEV<sub>1</sub> or FEV<sub>1</sub>/FVC ratio) may allow quantification of the 'asthmatic' contribution to symptoms, but without additional measurement of lung volume subdivisions the contribution of elevated BMI to respiratory symptoms cannot be estimated. Steier *et al* (2014) showed the elevated intra-abdominal pressure occurring in obese adults to be related to the degree of lung volume derangement, suggesting that measurement of lung volume may provide an estimate of the extent of respiratory load elevation occurring as a result of obesity. Further studies would benefit from examining the relative

contribution of both airflow obstruction and lung volume alteration to symptom severity in overweight asthmatic individuals. This would add to valuable work already undertaken investigating exercise responses in obesity alone and with concomitant lung disease, the findings of which support those of the current study. Ofir *et al* (Ofir *et al.*, 2007) demonstrated no differences in dyspnea-ventilation relationships between obese and healthy weight women, and suggested that the lower operating lung volumes may offer protection against breathlessness due to the greater capacity for tidal volume expansion. Romagnoli *et al* (2008) mirrored such findings, further supported by Ora *et al* (2011) in obese and non-obese patients with COPD. Salome *et al* (2008) showed that BMI did not have an independent influence on rate of change in Borg score during methacholine challenge testing in obese and healthy weight asthmatics. The results of these studies, together with that of the current work, support the premise of appropriate perception of increasing central respiratory drive in overweight and obese individuals. The contribution of baseline, underlying respiratory mechanical abnormalities is highlighted by our results, and should be considered when assessing respiratory symptom burden. It should be noted that an assumption of over-reporting of symptoms in this group may lead to suboptimal disease management by clinicians, indicating that further investigation in this area is warranted.

## **5. Conclusion**

This is the first study to examine respiratory load perception in overweight children with asthma. Our results suggest that the perceptual and objective responses to

increasing externally applied inspiratory load are not different between healthy weight controls, healthy weight asthmatics and overweight asthmatics. Overall perception scores were however higher in the overweight group, suggesting that the load placed on the respiratory system by elevated body mass may underlie the higher symptom burden associated with coexistent asthma and obesity.

#### **Conflicts of interest and funding**

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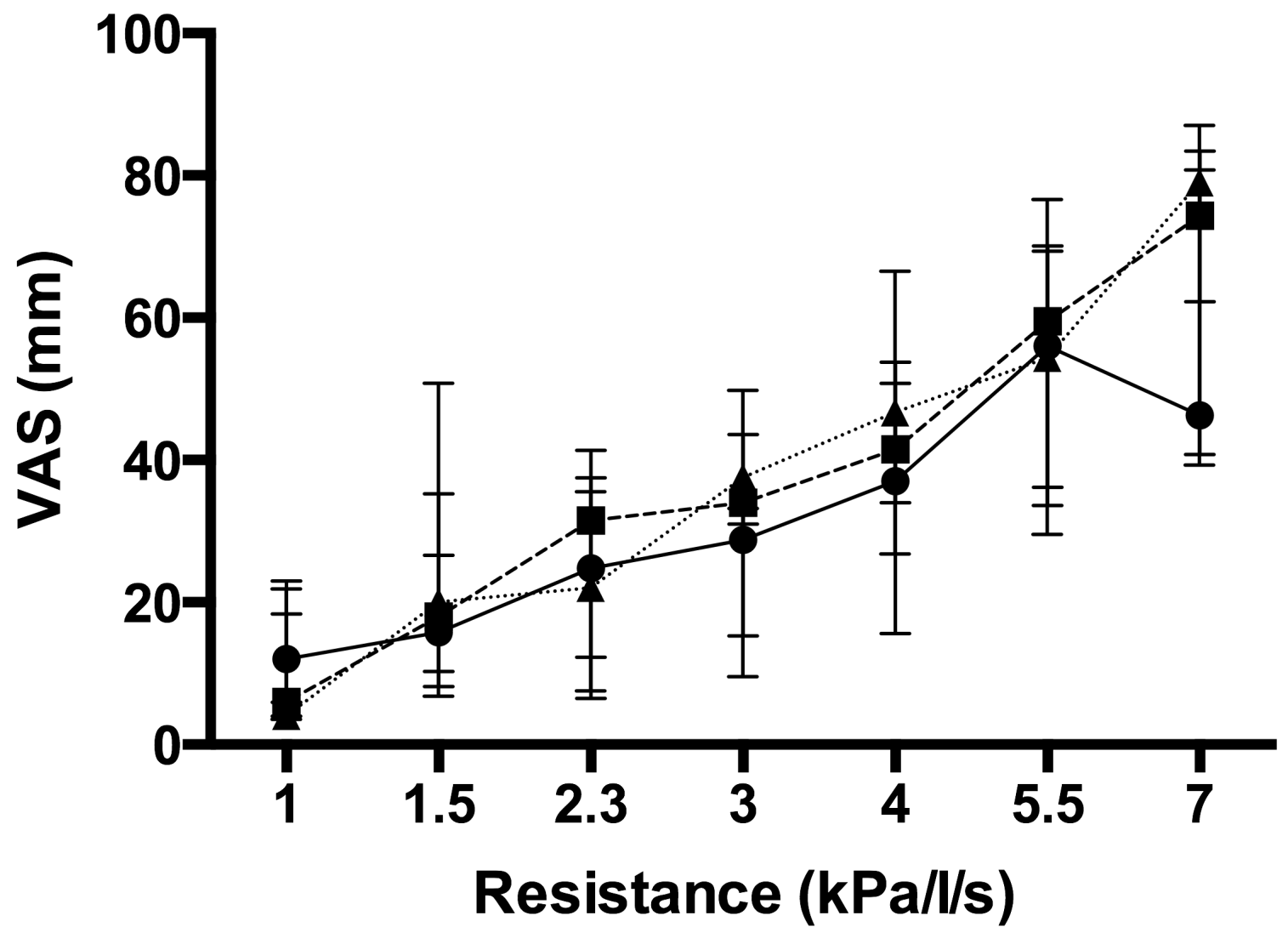


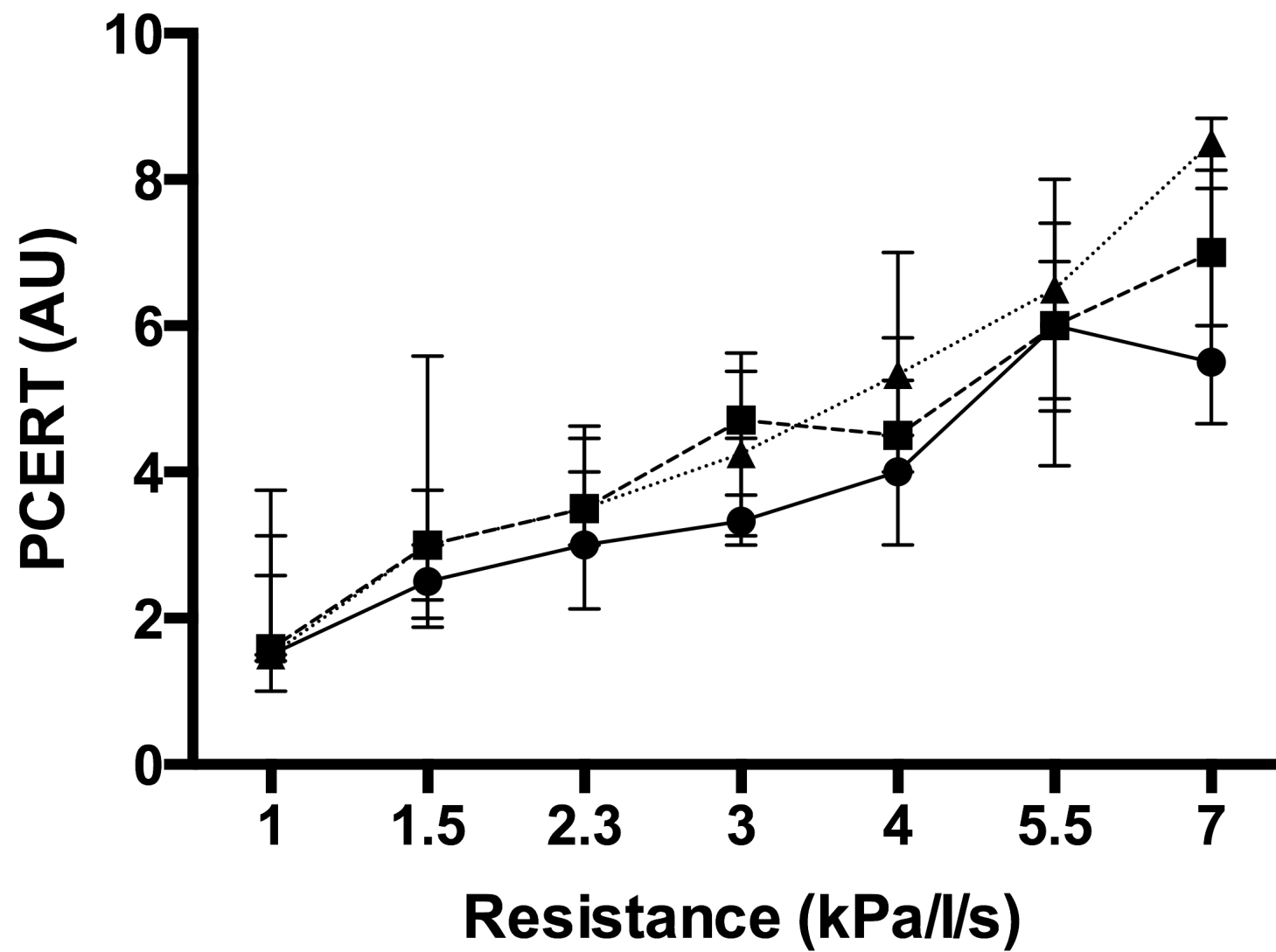
## Figures

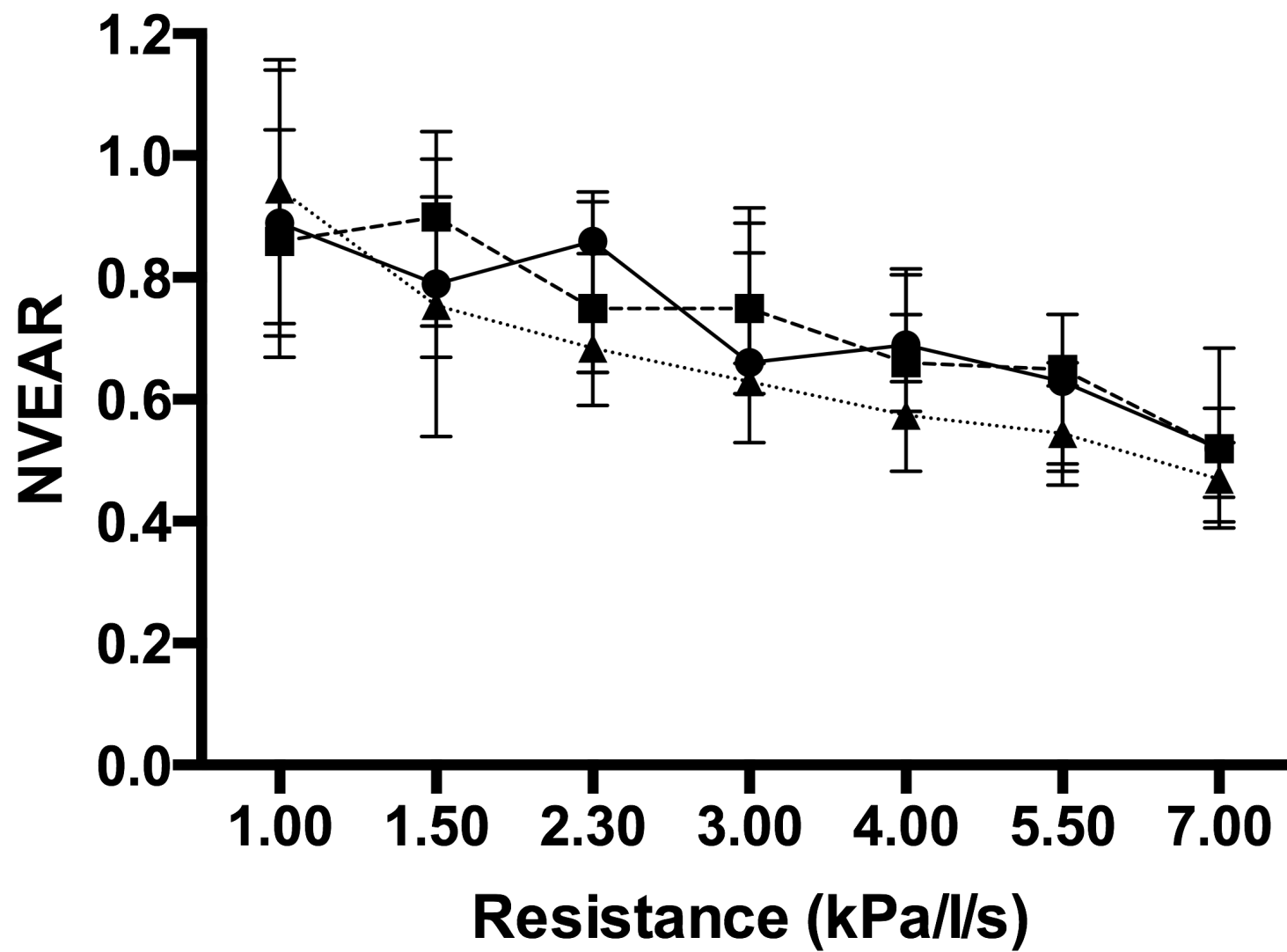
Figure 1 Visual analogue scale (VAS) values at each resistance level in 27 children undergoing inspiratory resistive loading. Circles/solid lines: healthy weight controls; squares/dashed lines: healthy weight asthmatics; triangles/dotted lines: overweight asthmatics.

Figure 2 Pictorial Children's Effort Rating Table (PCERT) values at each resistance level in 27 children undergoing inspiratory resistive loading. Circles/solid lines: healthy weight controls; squares/dashed lines: healthy weight asthmatics; triangles/dotted lines: overweight asthmatics.

Figure 3 Neuroventilatory efficiency activity ratio (NVEAR) at each resistance level in 27 children undergoing inspiratory resistive loading. All data expressed as a ratio of that at baseline (unloaded); the intercept term for the model was anchored at one. Circles/solid lines: healthy weight controls; squares/dashed lines: healthy weight asthmatics; triangles/dotted lines: overweight asthmatics.







## **Abstract**

Overweight asthmatic children report greater symptoms than normal weight asthmatics, despite comparable airflow obstruction. This has been widely assumed to be due to heightened perception of respiratory effort.

Three groups of children (healthy weight controls, healthy weight asthmatics, overweight asthmatics) rated perceived respiratory effort throughout an inspiratory resistive loading protocol. Parasternal intercostal electromyogram was used as an objective marker of respiratory load; this was expressed relative to tidal volume and reported as a ratio of the baseline value (neuroventilatory activity ratio (NVEAR)).

Significant increases in perception scores ( $p < 0.0001$ ), and decreases in NVEAR ( $p < 0.0001$ ) were observed from lowest to highest resistive load. Higher BMI increased overall perception scores, with no influence of asthma or BMI-for-age percentile on the resistance-perception relationships.

These data, indicating elevated overall respiratory effort in overweight asthmatic children but comparable responses to dynamic changes in load, suggest that the greater disease burden in overweight asthmatic children may be due to altered respiratory mechanics associated with increased body mass.

**Abstract word count: 160 words**

	<b>Controls (n=9)</b>	<b>Normal weight asthma (n=9)</b>	<b>Overweight asthma (n=9)</b>
<b>FEV<sub>1</sub> (L)</b>	2.25 (1.78 – 2.92)	2.34 (1.69 – 3.29)	2.43 (2.17 – 2.74)
<b>FVC (L)</b>	2.64 (2.01 – 3.42)	2.66 (1.89 – 3.99)	3.09 (2.73 – 3.47)
<b>FEV<sub>1</sub>/FVC ratio</b>	87.03 (83.27 – 89.36)	88.00 (81.33 – 89.16)	82.02 (78.30 – 83.31)
<b>TLC (L)</b>	3.17 (2.60 – 4.68)	3.51 (2.54 – 5.26)	4.00 (3.36 – 4.66)
<b>IC (L)</b>	1.28 (0.87 – 2.07)	1.70 (1.15 – 2.57)	2.05 (1.72 – 2.40)
<b>FRC (L)</b>	2.12 (1.38 – 2.97)	1.80 (1.43 – 2.47)	1.7 (1.58 – 2.30)
<b>RV (L)</b>	0.71 (0.54 – 1.19)	0.86 (0.69 – 1.10)	0.90 (0.77 – 1.14)
<b>RV/TLC ratio</b>	25.06 (18.80 – 26.00)	24.50 (22.51 – 27.18)	24.43 (19.17 – 26.26)

**Online supplementary material Table 1** Raw values for pulmonary function parameters.

**Highlights:**

- Excess awareness of respiratory effort is suspected in overweight asthmatic children
- Overall respiratory effort scores during resistive loading were related to body mass
- Dynamic responses to load were not influenced by asthma or overweight status
- Adverse respiratory mechanics may underlie higher symptom scores in overweight asthmatics
- These data refute the concept of altered breathlessness perception in this group